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Disease-a-Month

Dehydration

WALTER HOLLANDER, JR.
T. FRANKLIN WILLIAMS

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Dehydration

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The research and teaching interests of both authors have related particularly to problems of renal and body fluid physiology.

ON DECEMBER 29, 1831, William B. O'Shaughnessy, then recently out of medical school, wrote a now-famous letter (12). It read in part:

"1. The blood drawn in the worst cases of *the* cholera, is unchanged in its anatomical or globular structure.

"2. It has *lost a large proportion of its water,* . . .

"3. *It has lost also a great proportion of its* neutral *saline ingredients.*"

Soon after the details of Dr. Shaughnessy's brilliant studies were published, Thomas Latta, a medical practitioner, described what is believed to be the first instance of parenteral fluid therapy (11). Having read the report of O'Shaughnessy's work, Latta was stimulated to administer salt solutions in the "collapse" state of cholera. After trying the rectal and oral routes unsuccessfully, he "resolved to throw the fluid immediately into the circulation. In this, . . . I proceeded with much caution. The first subject . . . was an aged female, on whom all the usual

remedies had been fully tried, without producing one good symptom; . . . Indeed, so entirely was she reduced, that I feared I should be unable to get my apparatus ready ere she expire. Having inserted a tube into the basilic vein, cautiously—anxiously I watched the effects; ounce after ounce was injected, but no visible change was produced. Still persevering, I thought she began to breathe less laboriously, soon the sharpened features, and sunken eye, and fallen jaw, pale and cold, bearing the manifest impress of death's signet, began to glow with returning animation. The pulse, which had long ceased, returned to the wrist; . . . and in the short space of half an hour, when six pints had been injected, she expressed in a firm voice that she was free from all uneasiness, . . . her extremities were warm, and every feature bore the aspect of comfort and health . . ."

The patient described in this dramatic report subsequently died, but others who were similarly treated survived. The Lancet hailed O'Shaughnessy's studies and their rational application by Latta as great advances. "It teaches us how boldly we may proceed when certain and scientific data are before us . . ." (10).

Despite O'Shaughnessy's findings and their independent rediscovery and augmentation later in the nineteenth century, administration of parenteral fluids and the management of dehydration did not become accepted practice until the past 50 years. Now, however, the prevention and treatment of body fluid abnormalities has become one of the most important aspects of patient care, applicable in almost every branch of clinical medicine.

This article deals specifically with dehydration, which, as defined on page 17, generally involves losses of sodium and chloride ions as well as of water. It is important at the outset that the degree of precision desirable and necessary be put in proper perspective. Undoubtedly, many dehydrated patients are managed successfully by merely supplying adequate water and electrolytes and allowing the patient's own homeostatic mechanisms to make the needed adjustments. Whenever renal, adrenal and cardiovascular functions are reasonably normal, such an approach often proves adequate. However, many situations require the greatest possible precision for optimal management. Such an approach is not difficult once it has been learned and practiced; it does not require a specialist. However, it does require some understanding of body fluid physiology and of the pathophysiology as well as the various causes of dehydration. Each of these topics will be considered in turn in subsequent

sections. Lastly, as discussed in the final section (Management of Dehydration), it requires that this knowledge and understanding be applied as well as circumstances permit. Since the approach will be in part semiquantitative, some numbers and calculations will be necessary; however, the mathematics involved is all either simple arithmetic or elementary algebra.

Much of the discussion to follow necessarily represents a somewhat general consideration of body fluid physiology and its disorders. However, the organization and content have been selected *entirely* for their relevance specifically to dehydration. Many topics which belong in a general discussion of fluid and electrolyte disorders are not included here; more detailed accounts are given elsewhere (2, 3, 5, 7, 9, 14, 15, 17, 18, 19, 20, 21, 22). Where specific values are used, these refer to adults. Although the general principles are the same for children, the quantitative aspects are different (4, 7).

REVIEW OF BODY FLUID PHYSIOLOGY

Body Fluid Compartments

The normal adult body is 50-70% water, nearer the latter in a lean person, nearer the former in an obese one. This total body water (TBW) consists of the intracellular and extracellular fluids. The intracellular fluid (ICF) might be considered as multiple separate fluids, but for present purposes it can be thought of as one. The extracellular fluid (ECF) has two major subdivisions, the interstitial fluid (ISF) and the blood plasma. Quantitatively, the various major body fluid compartments are summarized in Table 1.

TABLE 1.—Compartments of Body Water

Compartment	Average Approx. % of Total Body Weight	Average Approx. % of Total Body Water
Total body water	60	100
Intracellular fluid	40	67
Extracellular fluid	20	33
Plasma	5	8
Interstitial fluid	15	25

Factors Controlling Distribution of Body Water

Osmotic considerations.—The many cell membranes separating intracellular and extracellular fluid are generally thought

to be freely permeable to water but not to most solutes. This is important in the analysis and correction of body fluid deficits, for reasons which depend on the process known as osmosis.

When a *solution* (water plus solutes) is separated from pure water by a membrane which is permeable to the water but to none of the solutes in the solution (a so-called semipermeable membrane), water will tend to move across the membrane from the water into the solution. This movement of water is known as "osmosis." The magnitude of the tendency for osmosis to occur depends on the total *number of solute particles* in a given volume of the solution. Each solute particle contributes to the osmotic activity of the solution, and therefore the total concentration of solute particles may be called the "osmotically active solute concentration." (This is strictly correct only in extremely dilute solutions, but it is an adequate approximation for use in this discussion.) Since each *particle* is osmotically active, the "osmotically active solute concentration" of salts which ionize in water is determined by the number of ions formed. Thus, one molecule of sodium chloride when dissolved in water forms two ions and hence two osmotically active particles.

Before proceeding further, terminology must be reviewed. Just as in traditional chemistry, a unit of measure is the "mol" (= molecular weight calculated as grams), the unit of measure in dealing with osmotic considerations has become the "osmol." This term is meaningful only when considering solutions, and in this context the following definitions are important.

1. For nonionized solutes in water solution (e.g., glucose or urea):
   One osmol = one mol = molecular weight as *grams*.
   One milliosmol = one millimol = molecular weight as *milligrams*.

2. For ions in water solution (e.g., Na^+, Cl^-, HCO_3^-, $HPO_4^=$):
   One osmol = ionic weight as *grams*.
   One milliosmol = ionic weight as *milligrams*.

3. $\text{Osmolarity} = \dfrac{\text{total number of osmols}}{\text{per liter of solution}} = \dfrac{\text{osmotically active}}{\text{solute concentration}}$ (approximate).

4. $\text{Osmolality} = \dfrac{\text{total number of osmols}}{\text{per 1,000 grams of water}} = \dfrac{\text{osmotically active}}{\text{solute concentration}}$ (more exact).

The term "osmotic pressure" is used widely in discussions of body fluid concentration. There are certain valid objections to its use in this way, and it seems preferable to refer either to

"osmolarity" or to "osmolality," which are both expressions of solute concentration as defined above. Both terms are sufficiently accurate in clinical situations; "osmolality" will be used in this discussion.

Osmosis occurs not only when water and a solution are separated by a semipermeable membrane, but also when two water solutions with unequal osmolalities are separated by such a membrane. Water will tend to move across the membrane in whichever direction and in whatever amount is necessary to equalize the osmolalities of the two solutions. As already implied, many biologic membranes are impermeable to some but not all of the solutes with which they are in contact. However, only the solutes which *cannot* traverse the membrane freely will contribute to the osmotic movements of water. A solute which can cross the membrane will do so until its concentration becomes the same on both sides. It will then add equally to the osmotically active concentrations of the two solutions. The term "effective osmolality" may be used for that part of the osmotically active concentration which is due to solutes that cannot traverse cell membranes freely. The osmotic contribution of urea, for example, is not part of the *effective* osmolality and does not influence the partition of body fluid because urea readily crosses cell membranes and its concentration is therefore the same in the intracellular and extracellular fluid.

The normal effective osmolality of body fluids is approximately 0.280 or 280 milliosmols per kilogram of water (mOsm./kg.) of water. The normal range is approximately 270—290 mOsm./kg. The term "isotonic" indicates a concentration in this range. "Hypotonic" means less than and "hypertonic" more than normal effective osmolality. Although not proved conclusively, it is presumed throughout this discussion that the effective osmolalities of the intracellular and extracellular fluids are equal.

STARLING FACTORS.—The distribution of water between plasma and interstitial fluid in any area of the body is governed by the four "Starling factors":

1. Hydrostatic pressure in the capillaries.
2. Colloid osmotic concentration of the interstitial fluid.
3. Tissue tension or pressure.
4. Colloid osmotic concentration of the plasma.

The first two tend to cause movement of water from plasma into interstitial fluid; the latter two have the opposite effect. The "colloid osmotic concentration" indicates that part of total

osmolality due almost entirely to protein. (It also includes a minor contribution due to small differences in ionic concentrations caused by differences in protein concentration, the Gibbs-Donnan effect).

Composition of Body Fluids

The average compositions of plasma and intracellular fluid are presented in Table 2. Concentrations are given both as milliequivalents (mEq.) and as milliosmols. The term "milliequivalent" applies only to *ions* and may be defined as follows:

$$1 \text{ mEq.} = \frac{\text{ionic weight as milligrams}}{\text{valence}}$$

Thus, milliequivalents depends on the total number of *charges*, whereas milliosmols depends on the total number of *particles*.

Plasma differs from interstitial fluid primarily because of the plasma proteins, the only constituent of plasma to which capillary membranes are not freely permeable. The composition

TABLE 2.—Composition of Plasma and Intracellular Fluid (5, 6, 9, 20)

Plasma

Cations	mEq./L. of Plasma	mOsm./L. of Plasma		Anions	mEq./L. of Plasma	mOsm./L. of Plasma
Sodium	132–142	132–142		Chloride	98–106	98–106
Potassium	3.5–5.0	3.5–5.0		Bicarbonate	25–29	25–29
Magnesium	1.5–3.0	0.75–1.5		Phosphate	1.6–2.8	0.8–1.4
Calcium	4.6–5.5	2.3–2.7		Protein	15–19	1–2

Intracellular Fluid (Muscle)

Cations	mEq./L. of Water	mOsm./L. of Water		Anions*	mEq./L. of Water	mOsm./L. of Water
Potassium	150	150		Phosphate†	110	?
Magnesium	40	20		Sulfate†	20	?
Sodium	10	10		Bicarbonate	10	10
				Protein†	60	?

*The osmotically active concentrations of the intracellular organic anions cannot be assigned because exact composition and ionic weights are not adequately defined.
†Mostly organic.

of most cells is unknown, and the figures given in Table 2 are those which seem to be approximately correct for skeletal muscle. It is thought that most cell membranes are not freely permeable to ions (electrolytes), glucose or protein, but are freely permeable to urea and dissolved carbon dioxide as well as to water. Substances which cannot traverse cell membranes freely may nonetheless cross them but only by active processes involving energy consumption.

Estimation of Body Fluid Osmolality

Sodium ions account for almost all of the cations in extracellular fluid. Hence, their concentration in serum is generally an accurate *index* of the effective osmolality of the extracellular fluid (and therefore of total body fluid). A change in the effective osmolality of body fluids is usually accompanied by a *proportional* change in the serum sodium concentration in the same direction.

The relationship between the serum sodium concentration and effective osmolality is extremely useful, but it is unreliable when there is significant hyperglycemia. The glucose in the extracellular fluid normally constitutes a relatively small component of the total effective osmolality, and its usual variations are so minor that they do not influence the distribution of body water significantly. However, when extracellular glucose concentration becomes abnormally high, the effective osmolality is thereby significantly elevated. This in turn causes an osmotic movement of water out of cells. This shift of water dilutes all constituents of the extracellular fluid including sodium, and hence the serum sodium concentration does not then accurately reflect body fluid osmolality.

Whenever it can be assumed that the serum glucose concentration is approximately normal, the relationship of the serum sodium concentration to the total effective osmolality of body fluids is expressed as follows*:

$$\begin{matrix}\text{effective} \\ \text{osmolality} \\ (\text{mOsm./kg.})\end{matrix} = 2\,[Na^+] + 6$$

where $[Na^+]$ = serum sodium concentration, mEq./L. of serum.

*The figure "6" is empirical and accounts for a normal glucose concentration, for other solutes with corrections (activity coefficients) necessary because the solution is not extremely dilute, and for the fact that $[Na^+]$ is the concentration of sodium in serum rather than in extracellular *water*.

When hyperglycemia exists, the glucose concentration must be included. Thus†:

$$\begin{matrix}\text{effective}\\ \text{osmolality}\\ (\text{mOsm./kg.})\end{matrix} = 2\,[Na^+] + \frac{\text{glucose} \times 10}{180} + 2$$

where glucose = serum glucose concentration, mg.% of serum.

†In the equation, glucose concentration is multiplied by 10 to convert it from milligrams per cent to milligrams per liter and is then divided by 180 (the molecular weight of glucose) to convert it to milliosmols per liter. The figure "2" is again empirical.

One other circumstance in which the serum sodium concentration is not a satisfactory index of effective osmolality is hyperlipemia. When of significant degree, hyperlipemia is usually recognized by lactescence of the serum. Details of this problem can be found elsewhere (20).

Normal Water Balance

Sources of water (Table 3).—Most water intake is voluntarily ingested and apparently is influenced by habit as well as thirst. In addition, the water content of food is greater than frequently appreciated and, similarly, all food *or tissue* yields water as an end product of its metabolism (oxidation). Finally, just as food contains water, the body tissues all have preformed

TABLE 3.—Normal Sources of Water

Form	Volume in Ml./24 hours
Ingested	Depends on thirst and habit; usually 500–1,500
Oxidation of food or body tissue	200–300
Preformed in food	600–1,000
Preformed water in body tissues*	Per gram of fat consumed—0.35 Per gram of muscle consumed—0.75

*Based on ref. 8.

water which becomes available whenever these tissues are utilized for energy, as in starvation.

Losses of water (Table 4).—There are certain losses of body water which represent an irreducible minimum.

1. *Insensible water loss,* or insensible perspiration, is a continuous loss of *pure* water from skin and lungs which, unlike sweat (sensible perspiration), does not involve active secretion. It is closely geared to body heat production and accounts for about 25% of the body heat lost.

2. *Sweat* is the body's principal source of heat loss when heat production exceeds the capacity of the other cooling mechanisms. In a normal, afebrile, inactive person in a temperate environment, sweat may be essentially nil. In contrast, a hard-working laborer or a febrile patient in a hot climate may sweat several liters per day. Unlike insensible perspiration, sweat always contains solutes, particularly sodium and chloride. The sodium concentration in sweat is quite variable, averaging 40-50 mEq./L. and almost never exceeding about 80 mEq./L. except in adrenal insufficiency and mucoviscidosis (cystic fibrosis of the pancreas). Hence, sweat is always hypotonic. The sodium content of sweat tends to be least after acclimation to hot weather or with sodium depletion.

TABLE 4.—NORMAL WATER LOSSES

FORM	VOLUME IN ML./24 HOURS
Insensible perspiration	600–1,000
Sweat (sensible perspiration)	Depends on need for heat loss; usually 100–1,000, occasionally much higher
Urine	Depends on solute load and water balance. Usual *minimal* volumes are (6):
	On normal diet 1,000
	Fasting 700
	On low salt, low protein, high carbohydrate diet 250–500

3. *Urine*: The minimal daily volume of urine depends on the quantity of solutes requiring excretion (urinary solute load) and the maximum concentration at which these solutes can be excreted in urine; i.e., the least amount of water required. The urinary solute load on usual adult diets (mainly urea, sodium ions and chloride ions) is in the range of 1,200 mOsm./24 hours (6), and the maximal urinary concentration 1,000—1,400 mOsm./kg. (specific gravity usually over 1.025); hence, the minimal urine volume is usually about one liter. Minimal urine volumes under certain other conditions are shown in Table 4. If the solute load requiring excretion is above average, as on a high-protein diet, during large-scale tissue breakdown, or when there is significant glycosuria, the minimal volume of urine is higher than normal. This illustrates the meaning of the term "osmotic diuresis" or "solute diuresis." The control of renal

sodium excretion, which greatly influences urine volume since it affects urinary solute loads, will be discussed later. Excess water can be excreted readily as a dilute urine up to quite large volumes in the range of a liter per hour.

4. *Gastrointestinal secretions:* The nature of gastrointestinal secretions must be understood since their loss is such a frequent concomitant of illness. The usual composition of the digestive secretions is presented in Table 5. The most important fact

TABLE 5.—COMPOSITION OF DIGESTIVE SECRETIONS (1, 20)

DIGESTIVE SECRETION	Na^+	K^+	HCO_3^-	Cl^-
	mEq./L.			
Saliva	8–38	13–24	4–20	9–18
Stomach	20–100	5–25	—	90–155
Bile	120–150	3–12	30–50	80–120
Pancreas	110–150	3–10	70–110	40–80
Small intestine	80–150	2–10	20–40	90–130

about them in relation to fluid balance is that, except for saliva, they are all *isotonic*. Except for gastric secretion, their principal cation is sodium at a concentration close to that in plasma. They all contain potassium and are therefore important potential sources of potassium depletion. In general, the secretions produced distal to the stomach are slightly alkaline. Gastric secretion, though variable, is commonly quite acid, with chloride as almost the only anion.

DAILY MAINTENANCE REQUIREMENTS.—The daily requirements for maintenance of fluid and electrolyte balance in a person with normal kidneys and no unusual losses, who is not ingesting food or water, can be estimated from Table 4. The minimal water requirement would be: 800 ml. for insensible perspiration and 700 ml. for urine—a total of 1,500 ml. However, this assumes maximal concentration of urine and no sweat. It is preferable to allow about 1,300 ml. for urine and 200 ml. for sweat—a total of 2,300 ml. Oxidation of administered carbohydrate plus the pre-formed water and water of oxidation of catabolized body tissues will provide about 300 ml. of water; hence, the total water that must be administered is $2{,}300 - 300 = 2{,}000$ ml. Although normal kidneys will not allow any serious sodium depletion to develop (in the absence of significant nonrenal losses), it is generally desirable to give 70-80 mEq. of sodium. To minimize catabolism and ketosis, at least 100 Gm. of carbohydrate must be supplied (6); to protect against potassium depletion, 30-50 mEq. of potassium should be included. All

these needs are readily supplied with 1,500 ml. of 5% dextrose in water, 500 ml. of 5% dextrose in isotonic saline, and 3 Gm. of potassium chloride (2,000 ml. of water, 75 mEq. of sodium, 100 Gm. of glucose, and 40 mEq. of potassium).

Normal Defenses Against Dehydration

There are three major defenses against dehydration: (1) thirst, (2) the ability of the kidney to produce urine with an osmolality 3-4 times that of the body fluids and (3) the ability

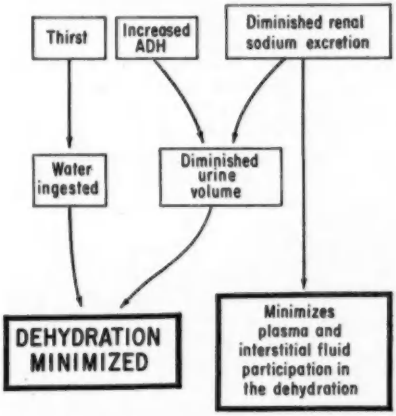

Fig. 1.—Defenses against dehydration.

of the kidney to produce urine essentially free of sodium and chloride. The manner in which each tends to minimize dehydration is diagrammed in Figure 1.

Thirst.—The mechanism of thirst is unsettled (9, 18, 20). It certainly involves local sensations in the mouth and throat and probably also includes a central nervous system mechanism for perceiving changes in body hydration. The primary stimulus for thirst is an increase in the effective osmolality of body fluids, as with water loss, with an excessive intake of sodium or with hyperglycemia. Thirst also appears to occur when there is a contraction of the extracellular volume or of some particular but unidentified portion thereof (18, 20). The well-known ob-

servation of thirst with hemorrhage suggests that the latter stimulus may depend on an intravascular site.

RENAL CONCENTRATING PROCESS.—The mechanism of the urinary concentrating process is not clearly understood. However, much is known regarding its *regulation*, which is largely con-

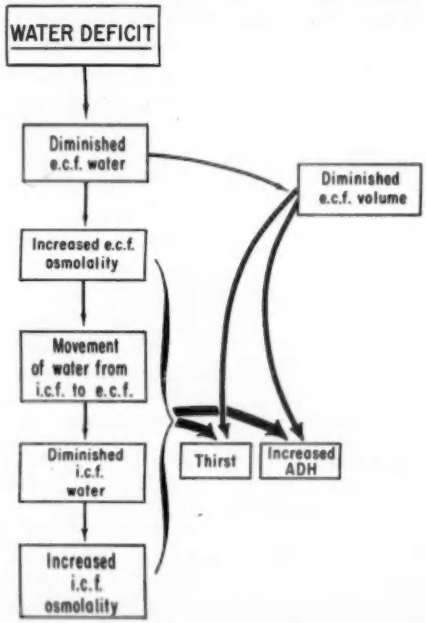

FIG. 2.—Physiologic stimuli of thirst and of antidiuretic hormone secretion.

trolled by antidiuretic hormone (ADH). The release of ADH from the neurohypophysis is, like thirst, primarily influenced by the effective osmolality of the body fluids. A rise in effective osmolality, as for example with a water deficit, induces increased release of ADH. This hormone is carried by the blood to the kidneys where, in some unknown manner, it causes the renal tubules to reabsorb more water without solutes and consequently to elaborate a more concentrated urine. A fall in effective

osmolality of body fluids generally has the reverse effect—a fall in circulating ADH and a consequently more dilute urine. Thus, this entire mechanism appears to have maintenance of normal effective osmolality as its *primary* purpose.

Another, less potent, physiologic stimulus which appears to increase the secretion of ADH is a reduction of the extracellular fluid volume (or some critical part thereof). Conversely, an expansion of this volume seems to suppress ADH secretion (16, 18, 20).

It is apparent from the foregoing discussion that thirst and the secretion of ADH are both induced by the same major factors. These are summarized in Figure 2.

Several other stimuli may cause augmented secretion of ADH and, since they are not part of the defense against dehydration, they may confuse the interpretation of a highly concentrated urine. These stimuli include: (1) emotional factors, particularly pain or fright; (2) nicotine; and (3) anesthetic and narcotic agents, including ether, the barbiturates and morphine. Alcohol is the one nonphysiologic stimulus which is known to *suppress* release of ADH.

RENAL SODIUM CONSERVATION.—Since the major ions of the extracellular fluid are sodium and chloride, their loss in any significant amount must have one or both of two serious consequences: (1) diminution of the extracellular volume (2) lowering of effective osmolality and consequent dilution and swelling of the cells. Either of these results is detrimental and potentially fatal if of major proportions. Hence, it is of great importance that the normal kidney can, when necessary, produce urine essentially free of these two ions. This fact depends on the ability of the renal tubules under appropriate stimuli to reabsorb all of the sodium and chloride which are filtered into them at the glomeruli. An amount of sodium equivalent to all that is normally present in the extracellular fluid is filtered at the glomeruli approximately every 2 hours; hence, sodium depletion could develop quite readily were its renal reabsorption imperfect. Indeed, as discussed later, this becomes a serious consideration in renal disease and in adrenal insufficiency. Ordinarily, a variable small percentage of the filtered sodium and chloride is excreted in the urine. The amount is exactly appropriate for the maintenance of sodium balance over the course of a day or so. The mechanisms regulating the renal excretion of sodium and chloride are incompletely understood (13, 14, 16, 18, 20). As with thirst and ADH secretion, alterations in the

volume of some component of the extracellular fluid seem to be one of the factors which influence renal sodium excretion (16, 18, 20) partly, but not entirely, through changes in adrenal cortical secretion. In many mammals, variations of glomerular filtration rate appear to play a major role in the control of sodium excretion. Whether this applies to humans is unsettled.

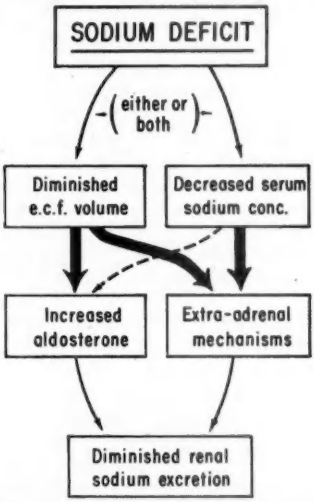

FIG. 3.—Outline of mechanisms by which a sodium deficit results in renal sodium conservation. The dotted line indicates that stimulation of aldosterone secretion by hyponatremia is doubtful.

For most clinical purposes, the following information suffices: If a normal person is placed on a sodium-free intake after he has been ingesting the liberal amounts of salt common in American diets (4-10 Gm.), he will produce an essentially sodium-free urine usually within 3-7 days, but in the interim will excrete some sodium and will consequently lose a minor amount of extracellular fluid, generally about one liter. Any significant reduction in the total sodium content of the extracellular fluid, whether manifested as a diminished extracellular volume, as a depressed serum sodium concentration or both, is ordinarily a potent stimulus for renal sodium conservation. A primary deficit

of water leads to renal sodium conservation despite an elevated serum sodium concentration, presumably due to the diminished extracellular volume. (18, 20).

Figure 3 summarizes the over-all mechanisms by which a sodium deficit (or a diminished extracellular volume due to a water deficit) leads to a diminished renal sodium excretion.

PATHOLOGIC PHYSIOLOGY OF DEHYDRATION

Definition and Terminology

Dehydration means loss of water, but for clinical purposes is best defined as a decrease in the volume of body fluid or of one of the major compartments of the body fluid. The use of "fluid" rather than "water" emphasizes the fact that solutes as well as water are usually lost. The most important and most commonly lost solutes are, of course, sodium cations and matching anions, generally chloride and/or bicarbonate.

As useful working terminology, it may be stated that the *net* losses of water and sodium are "equivalent" when the net loss has the same proportion of these as that which normally exists in the extracellular fluid; i.e., approximately 140 mEq. of sodium to every liter of water. It follows that water loss is greater than that of sodium when more than one liter of water is lost to each 140 mEq. of sodium lost. Conversely, sodium loss is greater than that of water when more than 140 mEq. of sodium are lost to each liter of water. Since this terminology refers to *net* losses, it is dependent on the intake as well as the output of sodium and water.

Sequence of Events and Quantitative Considerations

To understand the several clinical forms of dehydration, it may be helpful first to consider two rather extreme possibilities. Both these situations occur clinically, though more often there is a mixed condition representing some position intermediate between them.

Almost pure water deficit.—The first example is that of a patient with a deficit of water but with only a minor deficit of sodium and matching anions. This might occur in a person deprived of water and who had normal kidneys and no signifi-

cant sensible sweating or gastrointestinal losses. The sequence of events could be outlined as follows:

1. Net water loss in excess of water intake.
2. Diminished water content of extracellular fluid.
   A. Decreased extracellular fluid volume.
   B. Increased effective osmolality of extracellular fluid, thus creating osmotic inequality between extracellular and intracellular fluid.
3. Movement of water from intracellular to extracellular fluid until osmotic equality is re-established. This occurs continuously and hence osmotic inequality is never large.
4. Intracellular water diminished.
   A. Diminished intracellular fluid volume.
   B. Increased effective osmolality of intracellular fluid.

Thus, both the intracellular and the extracellular fluid share in this form of dehydration.

At some points in the sequence of events all three of the major defenses against dehydration would be stimulated. Thirst would lead to voluntary water ingestion if the patient were conscious and could drink; increased secretion of ADH would minimize water lost in urine; and renal sodium conservation would minimize contraction of the extracellular fluid specifically and would conserve water generally by decreasing the urinary solute load (see Fig. 1).

Some quantitative considerations of this type of situation may prove helpful (Table 6). Assume a 70 kilogram man who sustains a *net* loss of 5 liters of water without significant sodium loss. Before dehydration, total body water is 50-70% of body weight. If it is assumed that the patient is neither extremely lean nor fat, 60% of body weight is a reasonable estimate (Table 6, A). Intracellular fluid is about two thirds of total body water (B); the remaining third is extracellular fluid (C). The initial effective osmolality is presumed to be normal (D); this being so, the total effective solute in the extracellular fluid is determined by multiplying osmolality by the extracellular volume (E). Similarly, the total effective intracellular solute is calculated by multiplying osmolality by the intracellular volume (F). The total effective solute in all the body water is the sum of the preceding two results (G). However, this figure could have been more simply obtained by multiplying the osmolality times the volume of the total body fluid (H). If 5 liters were lost from the extracellular fluid *alone* and if there were no significant loss of sodium or anions, the extracellular fluid would be reduced from 14 to 9 liters (I) but would still contain the

same amount of solute; hence, its concentration would rise to a value determined by dividing the number of effective milliosmols by the new extracellular volume (J). At this point, effective osmolality of the extracellular fluid is much higher than that of the intracellular fluid. Actually, of course, this situation will never occur to this degree since water will come out of cells as

TABLE 6.—70 KG. MAN. WATER LOSS OF 5 LITERS. NO SIGNIFICANT SODIUM LOSS.

Before Dehydration

A. TBW = $70 \times 0.60 = 42$ liters
B. ICF = $42 \times 0.67 = 28$ liters
C. ECF = TBW − ICF = $42 - 28 = 14$ liters
D. Effective osmolality = 280 mOsm./kg.
E. Total effective solute in ECF = $285 \times 14 = 3{,}920$ mOsm.
F. Total effective solute in ICF = $285 \times 28 = 7{,}840$ mOsm.
G. Total effective solute in TBW = $3{,}920 + 7{,}840 = 11{,}760$ mOsm.
H. Total effective solute in TBW = $280 \times 42 = 11{,}760$ mOsm.

After Dehydration

I. ECF = $14 - 5 = 9$ liters
J. Effective osmolality = $\frac{3{,}920}{9} = 436$ mOsm./kg. } If no shift of water from ICF
K. Final TBW = $42 - 5 = 37$ liters
L. Final effective osmolality of TBW = $\frac{11{,}760}{37} = 318$ mOsm./kg.
M. Effective osmolality = $2\,[Na^+] + 6$
N. $[Na^+] = \frac{\text{Effective osmolality} - 6}{2}$
O. $[Na^+] = \frac{318 - 6}{2} = 156$ mEq./L.

soon as any osmotic difference develops. This osmosis will continue until osmotic equilibrium is re-established; hence, the final effective osmolality can be calculated by dividing total effective solutes by the final total body water (L). (It has been assumed that there is no significant change in the amount of solute but that total body water is diminished by 5 liters [K].) Knowing the effective osmolality, the anticipated serum sodium concentration can be derived (M, N, O) from the equation presented on page 9.

A reversal of the calculations just described is the process by which the magnitude of a water deficit may be approximately

defined in this type of clinical situation (Table 7). Given such a patient, it might well be possible from the history to guess that this was primarily a problem in pure water deprivation. In most such situations, the weight before dehydration would not be accurately known, but the current weight could be ascertained (A). The serum sodium concentration could be measured on a flame photometer (B). Effective osmolality could be calculated from the serum sodium concentration and assuming a normal serum glucose concentration (C). Total body water would have

TABLE 7.—DEHYDRATED PATIENT—SUSPECTED PRIMARY WATER DEFICIT

Calculation of Deficit

A. Body weight = 65 kg. (measured)
B. Serum [Na^+] = 156 mEq./L. (measured)
C. Effective osmolality = $2 \times 156 + 6 = 318$ mOsm./kg.
D. TBW = $65 \times 0.60 = 39$ liters
E. Total effective solute in TBW = $318 \times 39 = 12{,}402$ mOsm.
F. Desired effective osmolality = 280 mOsm./kg.
G. Desired TBW $\times$ 280 = 12,402
H. Desired TBW = $\frac{12{,}402}{280} = 44.3$ liters
I. Estimated water deficit = $44.3 - 39 = 5.3$ liters

to be approximated, and this could only be a guess based on the patient's general habitus and the degree of dehydration apparent from looking at him. In this case, the correct estimate would be somewhat less than 60% of body weight since 60% was assumed correct *before dehydration*. However, the physician could not know this and might well choose 60% as a best guess (D). (As noted later, this slight inaccuracy introduces a minor and unimportant error in the final estimate of the water deficit.) The total effective solute in the body fluids can be calculated—the total effective osmolality times the estimated total body water (E). In an equation analogous to (E) the "desired total body water" times the desired "normal" effective osmolality equals the total effective solute in the body fluids. The latter figure is assumed to be unchanged. The unknown is now "desired body water" (G) and can be calculated by rearrangement (H). To the extent that the problem represents a deficit of water without a significant deficit of solutes, as is being assumed, the quantity of water necessary to restore normal osmolality represents the total water deficit. The latter (I) is then simply the difference between the "desired total body water"

as determined in (H) and the estimated current total body water (D).

The final result of 5.3 liters is in error by 0.3 liters, according to the original assumptions, because of the slightly incorrect estimate of total body water. It is always necessary to make an intelligent guess regarding the volume of total body water, and fortunately, as illustrated here, the result is generally close enough for clinical purposes.

The calculations in Table 7 make use of the serum sodium concentration to estimate total effective osmolality, and the latter is used in subsequent steps. Essentially the same result can be obtained directly from the serum sodium concentration without calculating effective osmolality. This is shown in Table 8. Steps A and B and the estimation of total body water (C)

TABLE 8.—DEHYDRATED PATIENT—SUSPECTED PRIMARY WATER DEFICIT

Calculation of Deficit from Serum [Na^+]

A. Body weight = 65 kg. (measured)
B. Serum [Na^+] = 156 mEq./L. (measured)
C. TBW = $65 \times 0.60 = 39$ liters
D. Desired serum [Na^+] = 137 mEq./L.
E. Desired TBW × desired [Na^+] = Present TBW × present [Na^+]
F. Desired TBW $\times$ 137 = 39×156
G. Desired TBW = $\frac{39 \times 156}{137} = 44.4$ liters
H. Estimated water deficit = 44.4 — 39 = 5.4 liters

are the same as in Table 7. Obviously, from the equation used for calculating effective osmolality, the latter is closely reflected by the serum sodium concentration. Hence, instead of calculating effective osmolality and then the amount of water necessary to restore it to normal, it is just as satisfactory simply to calculate the amount of water necessary to restore the serum sodium concentration to normal. This is outlined in steps E, F and G. The important point to note is that, although sodium is limited largely to the extracellular fluid, these steps use *total body water*, not extracellular volume. Since any primary change in serum sodium concentration causes an osmotic shift of water into or out of the intracellular fluid, the serum sodium concentration can be restored to normal only when the effective osmolality of the total body fluid has been restored to normal. Similarly, it can be assumed that when the serum sodium con-

centration has become normal, effective osmolality will also have become normal.

ALMOST PURE SODIUM DEFICIT.—The other somewhat extreme type of dehydration is represented by a patient with a major deficit of sodium and anions but with a relatively minor deficit of water. This might occur in a patient who had lost large amounts of gastrointestinal fluids, as from diarrhea, and who

TABLE 9.—PATIENT WITH ALMOST PURE LOSS OF SODIUM AND ANIONS

Before Sodium Loss

A. TBW = $70 \times 0.60 = 42$ liters
B. ICF = $42 \times 0.67 = 28$ liters
C. ECF = $42 - 28 = 14$ liters
D. Effective osmolality = 280 mOsm./kg.
E. Total effective solute in TBW = $280 \times 42 = 11{,}760$ mOsm.

After Sodium Loss

F. Sodium loss = 600 mEq. = 600 mOsm.
G. Anion loss = 600 mEq. = 600 mOsm.
H. Total solute loss = 1,200 mOsm.
I. Water loss = 1 liter
J. TBW = $42 - 1 = 41$ liters
K. Total effective solute in TBW = $11{,}760 - 1{,}200 = 10{,}560$ mOsm.

L. Effective osmolality = $\dfrac{\text{Remaining effective solute}}{\text{Remaining TBW}}$

M. Effective osmolality = $\dfrac{10{,}560}{41} = 258$ mOsm./kg.

N. $258 = 2\,[Na^+] + 6$

O. $[Na^+] = \dfrac{258 - 6}{2} = 126$ mEq./L.

had received replacement fluid inappropriately as water rather than as isotonic sodium solutions. The initial sequence of events might be:

1. Large loss of isotonic sodium-containing fluid.
2. Replacement with equal volume of salt-free water; therefore—
3. Normal total body water but diminished extracellular content of sodium and anions.
4. Diminished extracellular sodium concentration.
5. Diminished effective osmolality of the extracellular fluid.

The diminished effective osmolality of the extracellular fluid has three significant consequences: (1) a shift of water from extracellular to intracellular fluid, (2) diminished thirst and

(3) diminished secretion of ADH. The latter results in somewhat more water being excreted in the urine, thereby reducing the water content and increasing the effective osmolality of the extracellular fluid. This, plus the decreased thirst, may at least partly offset the initial depression of extracellular osmolality, but with a consequently diminished extracellular fluid volume. If the sodium deficit were relatively minor, the extracellular effective osmolality might remain within normal limits and the final situation would be a minor reduction of extracellular volume without change of intracellular volume. However, if as postulated here the sodium deficit is large, the final condition will be both a diminished extracellular sodium concentration and some diminution in extracellular volume. Too much water is ingested and retained to maintain normal osmolality, but not enough to maintain a normal extracellular volume. Since the extracellular fluid is hypotonic, water moves from the extracellular to the intracellular fluid, and the latter is consequently expanded. (A low effective osmolality of the serum is almost always associated with overhydration of the intracellular fluid. "Asymptomatic hyponatremia," p. 39, may be an exception [19].)

Again, some quantitative considerations may be helpful (see Table 9 and text). Assume a 70 kilogram man with 42 liters of body water (A), 28 liters of intracellular fluid (B) and 14 liters of extracellular fluid (C). Before any derangement occurs, effective osmolality is normal (D), and total effective solute is the effective osmolality times the volume of body fluid (E). Assume a total loss of sodium ions of 600 mEq. (F) and the same loss of anions (G); the total solute loss is therefore 1,200 mOsm. (H). Assume in addition that body water decreases by one liter (I); then the final effective osmolality can be calculated by steps J, K and L, and the corresponding serum sodium concentration would be calculated in steps M, N and O.

Given this sort of problem in a patient, the available data are not ordinarily adequate to allow a simple reversal of these calculations to determine the deficits. However, it is possible to arrive at a useful first approximation for correction requirements. As demonstrated earlier, the serum sodium concentration is an entirely satisfactory index of the effective osmolality. Hence, the latter need not be calculated unless it helps clarify the reasoning for the reader. Henceforth in this discussion the serium sodium concentration will be used directly. Referring

to Table 10: the serum sodium concentration could be measured and would be 126 mEq./L. (A). The desired (normal) serum sodium concentration (B) minus the current measured serum sodium concentration gives the sodium concentration deficit (C). Since 1 liter of water had been lost, the patient's weight would be 69 kg. (D); from this, total body water could be estimated (E). The total sodium deficit must be *at least* the amount required to raise the serum sodium concentration to normal; hence, it must at least equal the sodium concentration deficit times the volume of body fluid (F). The result—455 mEq. of sodium—is below the originally assumed loss of 600 mEq. Had the 1-liter deficit of total body fluid been appreciated, as it might with accurate weights immediately before and after

TABLE 10.—DEHYDRATED, HYPONATREMIC PATIENT

Calculation of Deficit

A. Serum $[Na^+] = 126$ mEq./L. (measured)
B. Desired serum $[Na^+] = 137$ mEq./L.
C. Concentration deficit $= 11$ mEq. of Na^+
D. Body weight $= 69$ kg. (measured)
E. TBW $= 69 \times 0.60 = 41.4$ liters
F. Total sodium required to correct the serum $[Na^+]$ to normal $= 11 \times 41.4 = 455$ mEq.

the losses, a correct estimate of the total deficits would involve merely adding 1 liter (the fluid deficit) of an isotonic sodium solution to the above result. Thus, from Table 10 (F), 455 mEq. of sodium are needed to restore normal serum sodium concentration (and therefore normal effective osmolality). One liter of isotonic sodium solution represents approximately 150 mEq. of sodium; hence, the total deficit is $455 + 150 = 605$ mEq. of sodium plus equivalent anion. This is not significantly different from the originally assumed deficits.

The previous examples demonstrate that one can easily calculate the amount of water or sodium required to correct either hypernatremia or hyponatremia (and therefore either hypertonicity or hypotonicity of total body fluids). However, unless the water deficit is known from changes in body weight or from carefully kept fluid balance figures, it is impossible to calculate the entire alteration of body fluid. *In practice, it is usually desirable first to calculate and correct any abnormality of effective osmolality, after which the remaining deficit of body fluid*

has to be estimated from clinical appearance and other available data. This remaining deficit must then be corrected with increments of isotonic sodium solutions. (But see footnote on p. 40.)

Many instances of dehydration involve the loss of both water and sodium salts in significant amounts and hence represent varying mixtures of the two situations which have been analyzed in detail above. If the net loss of water and sodium were "equivalent" (as defined on p. 17), there would be no change in the sodium concentration of the extracellular fluid and therefore no change in the effective osmolality. In such a situation, the dehydration is borne entirely by the extracellular fluid. It is for this reason that isotonic sodium solutions should be used to correct any fluid deficit associated with a normal serum sodium concentration or remaining after the serum sodium concentration has been corrected to normal.

The various types of clinical dehydration can be summarized in terms of the compartments of body fluid involved:

1. Dehydration of both intracellular and extracellular fluid. This occurs when water loss is greater than sodium loss (or without sodium loss). Effective osmolality and serum sodium concentration increase. Thirst, ADH secretion and renal sodium conservation are stimulated. Example: Water deprivation.

2. Dehydration of extracellular fluid without change of intracellular volume. This occurs if water and sodium are lost "equivalently." Effective osmolality and serum sodium concentration do not change significantly. Renal sodium conservation is markedly augmented; thirst and ADH secretion are apparently stimulated if the condition is sufficiently severe. Examples: Some instances of diarrhea, the early stages of adrenal insufficiency, any residual fluid deficit after correction of hypo- or hypertonicity.

3. Dehydration of extracellular fluid with overhydration of the intracellular fluid. This occurs when sodium loss is greater than water loss (or without water loss). Effective osmolality and serum sodium concentration decrease. Physiologic defenses against dehydration are as in type (2). Examples: Acute adrenal insufficiency, sodium wasting due to renal disease.

4. Dehydration of the intracellular fluid with overhydration (expansion) of the extracellular fluid. This occurs when the concentration of sodium in the extracellular fluid is above normal due to an excess in the total amount of sodium and its

anions. Effective osmolality and serum sodium concentration increase. Thirst and ADH secretion are stimulated but renal sodium conservation is decreased. Example: Excessive administration of sodium chloride without equivalent water.

5. Dehydration primarily of the plasma. This tends to occur whenever the "Starling factors" are altered in such a direction as to cause a shift of water from plasma to interstitial fluid—this includes conditions involving increased capillary permeability to protein. Effective osmolality and serum sodium concentration do not change significantly. In many instances, associated renal sodium and water retention result in restoration of plasma volume to normal. Overhydration of the interstitial fluid (edema) is frequently present, and thus this finding cannot always be interpreted to imply adequate plasma volume. Examples: Burns; exudative skin disorders, some instances of the nephrotic syndrome, tourniquets.

The 4th and 5th items in this list would not always be considered examples of what is commonly meant by dehydration. They are included here for completeness and because they fit the broad definition of dehydration used in this discussion; i.e., a decrease in the volume of body fluid or of one of the major compartments of the body fluids.

Although the degrees of response vary, all three of the major defenses against dehydration are automatically stimulated in all the above situations with the single (and teleologically reasonable) exception that sodium excretion rather than conservation is stimulated by the condition outlined under type 4.

Figures 1, 2 and 3 have been combined in Figure 4 to summarize some of the physiologic consequences of dehydration and particularly the normal defenses which tend to minimize water and sodium deficits.

CAUSES OF DEHYDRATION

The causes of dehydration may be grouped under the general types of derangement in body fluid balance just described. With each cause, problems in diagnosis, prevention and management of dehydration which apply specifically to that situation will be discussed. The more general and systematic approach to evaluation and management of dehydration in any patient will be taken up later. Several references are pertinent to this and the next section (3, 4, 5, 7, 14, 17, 19, 20, 21, 22).

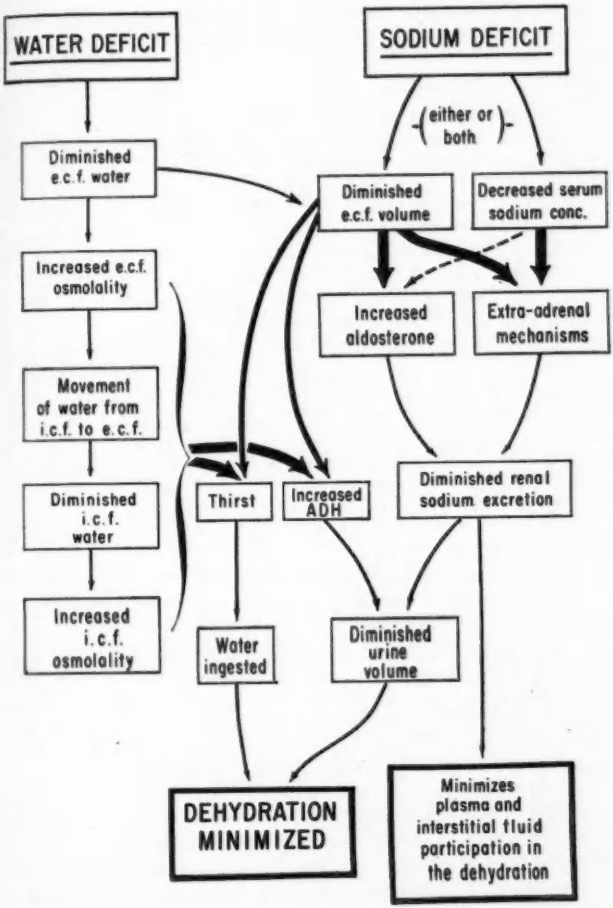

FIG. 4.—The major defenses against dehydration as physiologic responses to the loss of water and/or sodium.

Dehydration of Both Intracellular and Extracellular Fluids

(A deficit of water greater than the deficit of sodium)

Lack of ingestion of water.—This is likely to occur only when patients cannot care for themselves and in the rare patient who has lost the sensation of thirst. The problem arises in comatose patients, although the need for fluid administration is usually recognized here, and also in extremely sick patients whose oral intake frequently dwindles below minimal requirements.

Sweating.—Fever or exposure to intense heat can lead to the loss of large volumes of sweat. In addition, the *insensible* perspiration is increased somewhat by fever (about 50 ml./day/°F. rise in body temperature for adults). Inasmuch as sweat is hypotonic, the loss of water exceeds the loss of sodium. Nevertheless, the loss of sodium with any significant degree of sweating is too large to ignore. There is no adequate clinical method suitable for estimating the quantity of fluid lost by sweating. However, acute changes in body weight, unaccounted for by losses of other fluids may suggest losses by sweating. In composing a fluid for replacement of estimated losses in sweat, its sodium concentration may be assumed to be 40 mEq./L.

Renal losses primarily of water.—The kidneys may be unable to conserve water as well as normally for any of the following reasons:

1. *True diabetes insipidus.*—Lack of secretion of ADH. This may be the result of destruction of the neurohypophysis or its hypothalamic connections, and is characterized by polyuria, thirst with polydipsia and a constantly dilute urine. Urinary osmotic concentrations are well below that of the patient's plasma, and urine specific gravities are usually below 1.005. The criteria for this diagnosis are: (a) continued dilute urine despite hypertonicity of the body fluids produced by a deficit of water or by the infusion of hypertonic sodium chloride solutions (the Hickey-Hare test), (b) concentration of the urine to levels above that of plasma in response to vasopressin. This condition can be mimicked in patients who are polydipsic for neurotic or other reasons (primary polydipsia) and by diseases which impair the renal response to ADH. Inasmuch as urinary loss of water is the primary event, the finding of an elevated serum sodium concentration in a patient with polydipsia and polyuria would suggest diabetes insipidus or renal disease, rather than primary polydipsia. Enforced restriction of intake is occasion-

ally a part of the evaluation of polyuria. This must be done under constant observation; otherwise the patient may drink water and invalidate the test or, more important, dehydration may become severe enough to cause circulatory failure. Such restriction would also be potentially dangerous for any patient with renal impairment and should not be done until this has been excluded.

Theoretically, severe dehydration might produce an isotonic or slightly hypertonic urine in a patient with diabetes insipidus by causing a decreased glomerular filtration rate (20) but this could not be differentiated from incomplete diabetes insipidus.

2. *Inability of kidneys to respond to ADH* ("Nephrogenic diabetes insipidus").—This rare condition has a clinical picture like true diabetes insipidus except that the urine remains hypotonic even when vasopressin is administered. It has been recognized as an apparently congenital, hereditary anomaly with little evidence of other renal dysfunction. The same findings have been observed in obstructive uropathy and multiple myeloma.

3. *Chronic renal disease.*—Inability to concentrate the urine normally has long been recognized as a common feature of most types of chronic renal disease, although, as a distinguishing feature from diabetes insipidus, the kidneys can produce an isotonic or slightly hypertonic urine. This defect, in part at least, may be the result of a "solute diuresis" in the remaining functioning nephrons.

4. *Solute diuresis.*—Under any circumstance in which there is increased excretion of solutes in the urine, the minimal possible urine volume is increased (see p. 11). This is true because not only would more water be required at normal maximal solute concentrations of the urine, but also the maximal achieveable concentration declines with increasing solute excretion (3, 14, 18, 20). The two most common clinical conditions in which high urinary solute loads cause increased obligatory losses of water are the glycosuria of uncontrolled diabetes mellitus and the use of high-protein tube feedings. In diabetic patients with severe hyperglycemia, the glycosuria causes some increase in excretion of sodium as well as a diuresis. If acidosis is present, much more serious sodium losses will occur, which must be considered in the correction of the dehydration.

In reported cases of dehydration due to tube feeding, a high-protein mixture has been virtually the only source of water for these patients. The protein is metabolized largely to urea which,

on excretion, induces a solute diuresis. Often this cause of dehydration is unrecognized because large volumes of urine with specific gravities near 1.010 may lead the physician to think the patient is adequately hydrated. This problem need never arise if care is taken to use more dilute tube feeding mixtures, and the total water intake is adequate to allow for the excretion of urea. For every 100 Gm. of protein, 1,000 ml. of water *in addition to* the usual water requirements should be given.

With chronic renal impairment there is both clinical and experimental evidence that each remaining functioning nephron has an increased glomerular filtration rate and therefore an increased flow down the tubule. This is analogous to a solute diuresis and may explain in part the impaired ability to concentrate the urine. Furthermore, with azotemia, the elevated concentration of urea in the plasma ultrafiltrate as it enters the nephron would be expected to augment this solute diuresis.

5. *Depletion of potassium.*—There is now good evidence in humans and animals that depletion of potassium results in impairment of the urinary concentrating process. Potassium depletion may be the result of: any losses via the gastrointestinal tract including the habitual use of laxatives; losses via the urine due to congenital tubular defects, an oversupply of adrenal cortical steroids from external or internal sources and, rarely, acquired renal disease.

Dehydration of Extracellular Fluid with or without Expansion of Intracellular Fluid

(A deficit of sodium as great as or greater than that of water [Types 2 and 3 on p. 25]).

Losses via gastrointestinal tract.—Vomiting and diarrhea are the most frequent causes of dehydration. Other sources of gastrointestinal losses are gastric or intestinal suction and drainage from ileostomies, colostomies and any fistulous opening from the digestive tract. Since all gastrointestinal fluids are isotonic, their loss should cause a contraction of the extracellular fluid without significant change in the serum sodium concentration or of intracellular volume. However, frequently the patient with gastrointestinal losses has tried to ingest some fluids (usually water) or has been given some parenteral fluids (often predominantly dextrose in water) so that he has had a significant intake of water at a time when his losses are salt and water. The net result is a greater deficit of sodium than of water, a low serum

sodium concentration and an expanded intracellular volume. This illustrates the importance of considering intake as well as losses.

LOSSES OF SODIUM DUE TO RENAL DISEASE.—"renal salt-wasting." The normal kidney can conserve sodium to a remarkable degree, producing urine containing less than 1 mEq./L., when the stimuli for conservation of sodium are marked. In most forms of renal disease, this ability is impaired to varying degrees. The following conditions are worthy of special comment:

1. In the recovery phase of *acute tubular necrosis,* when the diuretic phase begins, the urine volume almost invariably becomes large with a sodium concentration of 30–90 mEq./L. Daily urine volumes of 5–6 liters or more are common, and thus as much as 500 mEq. sodium may be excreted per day. The kidneys only gradually recover their ability to elaborate a urine of a wide range of composition; the period of marked diuresis and large losses of sodium may persist for 3 weeks or longer. Therefore, during this period it is usually necessary to replace the urinary losses with an equal volume of water which contains sodium at an average concentration of 50–75 mEq./L.

2. Patients with *arteriolar nephrosclerosis* (the usual renal concomitant of essential hypertension), *chronic pyelonephritis* or *chronic glomerulonephritis,* are frequently unable to retain sodium normally. The defect in sodium conservation may be mild and therefore, on a modest intake of sodium, the patient may remain in balance and the defect unsuspected. However, a diet severely restricted in sodium may lead to a small daily negative balance which in time will be of significant proportions. Such a situation has been observed in the treatment of hypertension with rice diets or similar severely sodium-restricted diets. If such a diet is to be used in patients in whom impaired renal function is known or suspected, it is important to follow the patient closely and to measure the excretion of sodium in a 24-hour collection of urine after the patient has been following the diet 5–7 days. A fuller discussion of the indications for and precautions in measuring urinary sodium excretion appears on page 38. If the amount excreted is greater than the estimated content of the diet, then either the patient's intake of sodium is greater than the diet allows or he is developing a negative balance of sodium due to renal losses.

3. In patients with *obstructive uropathy,* the release of the obstruction is occasionally followed by marked polyuria with the excretion of relatively large amounts of sodium and, at

times, of potassium, even when the body has become depleted of sodium and the stimuli for its retention are presumably active. As in the recovery phase of acute tubular necrosis, this tends to be a transitory phenomenon.

4. A few patients have been observed whose renal losses of sodium were so great that the clinical picture was much like that of adrenal cortical insufficiency in crisis, with severe dehydration, circulatory insufficiency, hyponatremia, hyperkalemia and acidosis. Chronic pyelonephritis and congenital intramedullary cystic disease of the kidneys are two conditions with which this picture has been associated. These patients show little or no improvement in sodium retention with large doses of adrenal steroids, but the abnormalities in hydration and electrolye concentrations are reversed by supplying adequate amounts of sodium and, at times, small amounts of bicarbonate.

ADRENAL CORTICAL INSUFFICIENCY.—One of the major derangements in Addisonian adrenal insufficiency, the dehydration and its accompanying circulatory insufficiency, is due to excessive renal losses of sodium ions, chloride ions and water, to the transfer of sodium into body cells or bone and to minor losses of sodium in saliva and sweat. Frequently, these deficits are augmented by vomiting and diarrhea. The sequence of events is much like that described on pages 22-23. Initially, the net deficits of sodium and water are "equivalent," but eventually the net loss of sodium exceeds that of water and a significant fall in serum sodium concentration appears. The glomerular filtration rate falls, and azotemia may develop as a consequence both of contracted plasma volume and of some unexplained effect which is reversible by hydrocortisone. In addition, the ability of the kidney to excrete potassium, hydrogen and ammonium ions is impaired; hence, hyperkalemia and metabolic acidosis appear. These changes are the same as those frequently found in renal insufficiency, although in *adrenal* insufficiency both the acidosis and azotemia tend to be mild, and renal loss of sodium is usually more severe. Other clinical features will generally point to the correct diagnosis, but occasionally differentiation between adrenal cortical and renal insufficiency is quite difficult.

CEREBRAL SALT-WASTING (19, 20).—A few patients with various cerebral lesions have developed, apparently rather suddenly, extremely high rates of renal excretion of sodium and chloride ions. Losses as high as 600–900 mEq. of sodium per day have been recorded. The urinary concentration of sodium is usually

hypertonic and such patients are frequently receiving more water than salt. Thus, deficits of sodium exceed those of water. Severe dehydration, hyponatremia and circulatory collapse all develop rapidly if the condition is not recognized and treated promptly. The passage of large volumes of urine and the appearance of dehydration in a patient with a cerebral lesion who has been receiving a normally adequate fluid intake should alert the physician to the probability that this condition, or diabetes insipidus, is present. Determination of the serum sodium concentration and the rate of urinary excretion of sodium will establish or exclude cerebral salt-wasting. Replacing the deficits of sodium and water and continuing then to match output by intake will alleviate this part of the problem. In those patients who have survived their basic disease for some time, the salt-wasting has disappeared in a few days to 2–3 weeks.

Dehydration Primarily of the Plasma Volume
(Type 5 of the classification on p. 26.)

This type includes losses from inflamed areas, such as burned or avulsed areas or in certain dermatologic conditions—pemphigus, erythema multiforme bullosum, exfoliative dermatitis and rarely bullous dermatitis herpetiformis. Losses from such areas have nearly the same composition of sodium, water and protein as the plasma. There results primarily a contraction in plasma volume, although significant losses of interstitial fluid may occur as well. The danger of circulatory insufficiency is thus great, and some form of plasma-expanding solution should be included among the replacement fluids. The volume lost is difficult to estimate accurately, and the amount of replacement fluids to be given must be continually reassessed in the light of the patient's clinical signs.

Losses as a result of thoracenteses, abdominal paracenteses or the use of Southey's tubes may occasionally lead to this type of dehydration. The removal of fluid from pleural or peritoneal spaces or, rarely, from the subcutaneous tissues of the legs, is sometimes helpful in the management of patients with various diseases which can cause such collections of fluid. Furthermore, these fluids, "sequestered" portions of the extracellular fluid, are not readily available to the rest of the body, and one would think that their removal would have no ill effects. However, unless influenced by other therapeutic measures, the conditions

which created these fluids almost invariably still exist. The equilibrium is so delicately balanced that the removal of some fluid is immediately followed by the movement of more fluid from the plasma volume into the sequestered space until a state of equilibrium is reached again. If large amounts are removed rapidly, the loss of fluid from the plasma may produce circulatory insuffi-

TABLE 11.—CAUSES OF DEHYDRATION

A. *Dehydration of both intracellular and extracellular fluids—deficit of water greater than deficit of sodium.*
   1. Lack of ingestion of water.
      a. General depression of central nervous system.
      b. Damage to "thirst center."
   2. Sweating, due to fever or external heat.
   3. Renal losses primarily of water.
      a. True diabetes insipidus.
      b. "Nephrogenic diabetes insipidus."
      c. Chronic renal disease.
      d. Solute diuresis, especially diabetic glycosuria and high-protein tube feeding.
      e. Depletion of potassium.

B. *Dehydration of the extracellular fluid with or without expansion of intracellular fluid—deficit of sodium as great as or greater than deficit of water.*
   1. Losses via the gastrointestinal tract.
   2. Losses of sodium in renal disease.
      a. Recovery phase of acute tubular necrosis.
      b. Chronic parenchymatous renal diseases.
      c. Obstructive uropathy.
   3. Adrenal cortical insufficiency.
   4. Cerebral salt-wasting.

C. *Dehydration primarily of the plasma volume.*
   1. Losses from inflammed or burned areas.
   2. Removal of sequestered fluid.

ciency. This sequence has been best documented in patients with cirrhosis and ascites following abdominal paracentesis, but it has been observed with the removal of fluid from other areas as well.

A striking example was a 19-year-old male with the nephrotic syndrome with massive anasarca. After all simpler attempts to reduce the edema had failed, the insertion of Southey's tubes in his legs was followed by the loss of 37 liters of fluid in 6 days. At the end of this time, he was virtually free of edema, but he was very thirsty, his pulse had risen, pulse pressure had narrowed, and his NPN had

risen from about 40 to 97 mg.%. It seems almost certain that at this point his plasma volume was seriously contracted.

The dangers of such contractions of plasma volume can be avoided by removing relatively small amounts of fluid at any one time (2–5 liters from the peritoneal cavity and, for other reasons, usually no more than 1 liter from the pleural cavity), and by close observation of the patient for 12–18 hours following paracentesis. If evidence of circulatory collapse begins to develop, a plasma-expanding solution should be given promptly. It may be advisable, in patients with particularly low concentrations of serum albumin, to give human serum albumin or dextran solutions in isotonic saline (which carry no risk of transmitting serum hepatitis) during and after the paracentesis.

Rarely, a patient with hypoalbuminemia (nephrotic syndrome or cirrhosis) may develop signs of circulatory failure when placed on a low-sodium intake or given diuretic agents. Such an event may represent contraction (dehydration) of the intravascular volume due to renal losses of sodium and water even though the total extracellular volume may be normal or large.

Table 11 summarizes the causes of dehydration just discussed. In evaluating a patient with dehydration, the attending physician should consider these possible causes systematically. Management of the patient would then include attention to the underlying diseases as well as management of the dehydration.

STEPS IN RECOGNITION, EVALUATION AND MANAGEMENT OF DEHYDRATION

Features which Suggest Dehydration

Any of the following clues should alert the physician to the possibility that a patient is dehydrated:

1. History of unusual losses of fluids—profuse sweating, vomiting, diarrhea, passage of large volumes of urine, drainage from an inflamed area.
2. History of poor intake of fluids.
3. Complaint of thirst.
4. Findings on physical examination of poor turgor to the skin, a dry and particularly a shrunken, pointed tongue, soft eyeballs.
5. Laboratory findings of unexpectedly high values for hemoglobin concentration, hematocrit, concentration of total serum

protein, or concentration of sodium in serum; an unusually low serum sodium concentration; a high specific gravity of the urine. None of these laboratory findings alone can establish the presence of dehydration, for any of them can have other explanations.

Evaluation of the Dehydrated Patient

Once the suspicion of dehydration has been aroused, the evaluation of this problem should follow two lines: (1) a systematic search for the cause of the dehydration as already discussed and (2) an attempt to estimate the nature and quantities of the patient's deficits of water and electrolytes and thus his immediate needs. Such an estimation is the most important single step in the management of dehydration, for the choice of fluids to be given grows logically and simply out of this evaluation.

Historical data.—A valuable and frequently neglected part of the estimation of deficits is the collection and tabulation of all available historical data on the nature and amounts of the patient's intake and output since he was last normally hydrated. When the patient has just come under medical care, this information, obtained from the patient and his family, will usually be semiquantitative at best. Even so, fairly good guesses about losses and intake can often be made. Dehydration often develops in the hospital, and here the hospital records of intake and output, weight, nature of fluids given, nurses' notes, etc., will usually enable the physician to reconstruct a more exact record of fluid and electrolyte balance. Whenever dehydration has developed, or whenever it is thought that fluid and electrolyte balance *may become* a problem, a table of intake and output should be prepared and kept up to date.

An appropriate form for tabulating data of importance in fluid balance problems can easily be prepared and used in a patient's hospital record, or with patients being cared for at home. The following headings and additional columns for hemoglobin, hematocrit and serum electrolyte concentrations should be included:

		Intake		Output				
Date	Weight	Volume	Approx. Na.	Estimated Insens. Persp.	Urine Volume	Other Losses	Total Volume	Approx. Na.

"Other losses" would include sweat and gastrointestinal losses. The estimation or determination of urinary content of sodium

is discussed later. In such a table the intake and output can be totaled and an estimate of the net balance of water and sodium can be obtained. The changes of body weight, if known, serve as a check on the accuracy of the fluid balance calculated from intake and output.

PHYSICAL FINDINGS.—The physical signs of dehydration may give a semiquantitative estimate of its degree. Except in old or debilitated persons in whom this finding may be unrelated to dehydration, even mild *loss of skin turgor* is a valuable guide to the presence of significant dehydration. Normally, when the skin of the body is picked up in a small pinch and then released, it almost instantaneously resumes its usual state. When turgor is poor, the skin will remain wrinkled and folded for varying periods and only gradually resume its normal shape. Severe dehydration is suggested by evidence of inadequate circulating blood volume, such as tachycardia, narrow pulse pressure, hypotension, cold or blotched extremities, when no other cause for these findings is present.

LABORATORY TESTS.—Laboratory examination of the patient's blood and urine are usually indispensable in estimating the dehydrated patient's status when first seen and during therapy. The concentration of *hemoglobin* and *packed cell volume* (hematocrit), and the concentration of *total protein* in the serum would be expected to be above the patient's predehydrated levels. (In patients with previous anemia, "normal" values would be abnormally high.)

The concentration of the urine, as reflected by specific gravity or determined more accurately by depression of freezing point, is often extremely helpful. The combination of low urine flow and a high specific gravity strongly suggests dehydration. However, other conditions can also produce this combination, including congestive heart failure, acute glomerulonephritis, cirrhosis, the nephrotic syndrome or any of the nonphysiologic stimuli to ADH listed on page 15. Patients who seem clearly dehydrated but whose specific gravities are in the intermediate range of 1.005–1.015 may be suspected of having either renal impairment (including acute tubular necrosis) or a solute diuresis. A specific gravity of 1.005 or lower suggests either that a patient is adequately hydrated or, if dehydrated, that he has true or "nephrogenic" diabetes insipidus.

When glucose or certain other solutes (such as Diodrast®) are present, the specific gravity may be high even though the urinary osmotic concentration is not; hence, a high specific

gravity under these circumstances may not imply maximal urinary concentration.

Other abnormal urinary findings such as albuminuria, cells, casts or bacteria, may point to renal disease as a cause of the dehydration. However, mild albuminuria and casts are often found in dehydration alone.

The determination of the *urinary content of sodium* is important if one suspects that urinary losses of sodium (when they cannot be adequately estimated) are contributing to the dehydration. This is true in the following situations:

1. *Unexplained* dehydration with a normal or low serum sodium concentration, particularly the latter. The suspicion of urinary sodium loss would be even greater if the urine volumes were normal or large despite the dehydration. In particular, when patients on low sodium intake develop dehydration or hyponatremia, one should suspect, until proved otherwise, that urinary losses of sodium are exceeding intake.

2. The situation of the patient in whom the suspicion has been raised on grounds other than dehydration that he might have salt-wasting via the kidneys and thus might become dehydrated. Included in this group are patients suspected of having Addison's disease, cerebral salt-wasting or patients with hypertension or renal disease who are being considered for a low sodium diet.

When measuring the renal excretion of sodium, one must have a timed collection (usually 24 hours) for determination of amount of excretion as well as concentration of sodium. The significance of the amount of excretion depends on whether it is greater than the intake; therefore, the latter must also be known during the same period. If hyponatremia and dehydration (which would imply a strong stimulus for renal sodium conservation) persist throughout a urine collection, the excretion of more than 10–15 mEq. sodium per 24 hours would suggest abnormal renal losses regardless of intake. In emergency situations valuable information about the patient's dehydration may be gained from a single determination of urinary sodium concentration in a brief collection, i.e., the initial urine obtained on admission or, if possible, a timed 1–2 hour sample. A low concentration (5–15 mEq./L.) or low total amount of sodium in such a sample would be evidence against abnormal urinary losses.

The determination of the *concentration of sodium in the serum* is the most helpful of the blood chemical tests in evalu-

ating the dehydrated patient and is almost indispensable for estimating replacement of losses. As has been pointed out, the serum sodium concentration will not indicate the total amount of loss of sodium. However, if one can make a reasonable estimate of the total deficit of fluid and also knows the serum sodium concentration, one can calculate the composition of fluids to be given to restore, first, normal effective osmolality of body fluids and, second, what appears clinically to be a state of normal hydration. The examples on pages 20, 24, 44 and 46 illustrate the calculations involved. Two possible pitfalls in interpretation of serum sodium concentration have already been indicated: hyperglycemia or marked hyperlipemia.

The foregoing discussion of serum sodium concentration should not mislead the reader into thinking that hyponatremia always indicates dehydration. Clearly, hyponatremia can be produced by overhydration with water. In addition, it is found in certain patients with chronic debilitating diseases who are not dehydrated and who show no other ill effects of the hyponatremia. The latter condition is frequently called "asymptomatic hyponatremia" or "sick-cell syndrome." The diagnosis of asymptomatic hyponatremia is not always clear-cut and it may be necessary to correct the serum sodium concentration as a therapeutic trial (19, 20).

If acid-base balance and renal function are normal, the serum sodium concentration may be estimated by the sum of concentrations of chloride and carbon dioxide content (as mEq./L.) plus 10. Unfortunately, when this estimation would be most valuable these conditions are often not met or are difficult to evaluate. Hence it is far preferable to have a direct measurement of serum sodium concentration.

Among the other chemical determinations of the blood or serum, the BUN or NPN, if elevated, would suggest the presence either of renal disease which might cause a patient's dehydration, or a degree of dehydration severe enough that the glomerular filtration rate is depressed.

The *concentration of potassium in serum* should be determined in any problem of dehydration since, as already discussed, there may be associated deficits or elevated serum concentrations of this ion. Similarly, *acid-base disturbances* frequently accompany problems in dehydration and therefore often need evaluation. These topics, too large to cover here, are discussed elsewhere (3, 17, 19, 20, 21, 22).

If severe dehydration is present, treatment should be started at once with isotonic saline. More precise replacement can then be planned.

In less urgent situations, once the nature and quantities of the patient's deficits have been determined as accurately as possible, the aim of fluid therapy becomes replacement of these deficits and prevention of further deficits. As already discussed, a logical approach is, first, to return the effective osmolality (as reflected by serum sodium concentration) to normal and, second, to replace any remaining deficits of fluid with isotonic sodium solutions. When water deficit exceeds that of sodium, the first step involves the administration of enough water to lower the serum sodium concentration to normal, as in the example on page 21.* When the sodium deficit exceeds that of water, the first step involves the giving of enough sodium in excess of water to raise the serum sodium concentration to normal, as in the example on page 24. This approach is particularly important when the deviation of serum sodium concentration from normal is more than a few mEq./L. When the serum sodium concentration is normal initially, the problem is simply one of replacing the fluid deficit as an isotonic sodium solution.

This attempt at a quantitative approach to replacement depends for its safety and value on accurate laboratory determinations and calculations. If any feature of the clinical picture raises doubt about this accuracy, then clearly the first step is to repeat the determinations and calculations. Similarly if, as often happens, an abnormal laboratory result is first recognized a number of hours after the blood sample was obtained, the determination should be repeated before using it as a basis for calculation.

Often the parenteral route must be used and in order to be able to compose the proper mixtures of replacement fluids the following readily available solutions are needed:

1. Dextrose, invert sugar and/or fructose in water (5% and 10%).
2. Isotonic sodium chloride (0.9%) (154 mEq. Na^+/L.).

*It appears that, in children (particularly infants) rapid restoration of normal tonicity with solute-free water may cause convulsions. Hence, in *pediatric practice*, it is probably wiser to correct dehydration and hypertonicity by administering some sodium simultaneously with water from the outset. This can be done, for example, with a solution which is one third isotonic saline and two thirds 5% dextrose in water.

3. Hypertonic sodium chloride solution (3%—512 mEq. Na^+/L. or 5%—855 mEq. Na/L.)

4. Sodium bicarbonate in sterile vials (7.5%) (approximately 900 mEq. Na^+/L.)

5. Sterile solutions of potassium chloride or other potassium salts (a suitable preparation from which measured amounts may be added to other bottles of infusion is one containing 2 mEq. of potassium per ml. in 20–50 ml. vials).

The two examples under Pathologic Physiology of Dehydration will serve to illustrate the choice of fluids for replacement of deficits. In the first example (p. 21), the amount of water needed to restore the serum sodium concentration to normal was estimated to be 5.4 L. The first step in the therapeutic plan might therefore be to give 5–5½ liters of dextrose in water. The dextrose would be metabolized and the net effect would be the addition of the water. Water given parenterally must of course always contain some osmotically active solute which does not *diffuse* across cell membranes, such as sodium salts or sugars. In this simple example the deficit in water was the only deficit and therefore no further fluid would be needed to restore the patient to a state of normal hydration.

In the second example (p. 24), the amount of sodium needed to restore the serum sodium concentration to normal was estimated to be 455 mEq. The first step would therefore be to give this as a hypertonic sodium solution. If there were no derangement of acid-base balance it would be satisfactory to give the entire 455 mEq. as sodium chloride. One might therefore use 5% sodium chloride solution (855 mEq. Na/L.); the volume needed to supply 455 mEq. is:

$$\frac{455}{855} = 0.533 \text{ L. or } 533 \text{ ml.}$$

If, after correction of the serum sodium concentration, it was estimated on available evidence that the patient still had a deficit of fluid, the additional fluid would be given as an isotonic sodium solution. In the example given, it was estimated that the patient had a 1-liter fluid deficit. Thus, the second step in replacement would be to give a liter of isotonic sodium chloride. If metabolic acidosis were present in this example, it would be desirable to give some of the sodium as bicarbonate. If it were decided to give half of the hypertonic sodium solution as bicarbonate and half as chloride, the calculated amounts are:

$$\frac{455}{2} = 227.5 \text{ mEq. of each;}$$

$$\text{Amount of 5\% NaCl} = \frac{227.5}{855} = 0.267 \text{ L. or 267 ml.}$$

$$\text{Amount of 7.5\% } NaHCO_3 = \frac{227.5}{900} = 0.254 \text{ L. or 254 ml.}$$

One necessarily gives a significant amount of water with hypertonic sodium solutions—about 540 ml. in the last example. This water should be included in the fluid balance figures.

The use of hypertonic sodium chloride intravenously deserves special comment. Its administration, by causing water to shift from cells to the extracellular fluid, results in an expansion of the extracellular fluid out of proportion to the volume administered. This as well as the concomitant decrease in the intracellular fluid volume is one of the desired effects of its use. However, particularly if cardiac failure might be incipient, this expansion of extracellular volume should be produced slowly. It is therefore best to give hypertonic sodium chloride slowly, with frequent observation, preferably in quiet surroundings to a sedated patient. In addition, since the infusion may transiently induce thirst, it is usually necessary to restrict all other fluid intake (except isotonic sodium solutions or a volume of water calculated to replace insensible loss and urine) during and for 6–12 hours after giving the hypertonic solution. Otherwise, the patient may ingest excessive amounts of water and thus prevent the desired correction of osmolality.

Various "physiologic" solutions are offered commercially as specific replacement for specific types of losses. However, no standardized solution is likely to be suitable replacement therapy for a specific patient; each patient's needs must be evaluated individually according to his own *net* deficits. With the simple solutions listed above, the replacement needs of almost any patient can be met. On some occasions, there are special indications for the use of calcium, magnesium and phosphate, which can be added accordingly.

Although isotonic saline may be given safely by hypodermoclysis, solutions of dextrose in water or dextrose plus saline may be hazardous if administered by this route since this may temporarily contract the plasma volume (19, 20).

It is almost always possible to correct fluid deficits within 24 hours. But the patient continues to lose fluids during the period of correction; allowances should be made for these losses.

During the course of replacement it is necessary to reassess the patient's status. Certainly, by the time that half of the replacement fluid has been given, the physician should satisfy himself that his original plans are still reasonable. When the calculated fluids have been administered, the situation should be re-evaluated with appropriate clinical and laboratory observations. Because dehydration with its accompanying circulatory impairment can itself be a cause of acute renal tubular necrosis, another examination of the urine as well as a record of total output is important. At each stage of replacement therapy, all of the data should "add up"; that is, the patient's state of hydration should appear appropriately improved, the positive balance of fluids should equal the weight gain and the final serum sodium concentration should be the predicted one within a few mEq./L. If this is not true, one or more of the following possibilities should account for the discrepancy: a laboratory error, an error in weighing, an incorrect calculation, unexpected or unrecorded losses of fluid or errors in recording fluid intakes.

Any patient who is sick enough to develop dehydration requires daily reassessment of his state of hydration until the underlying disease has been resolved or has become stabilized. The value of maintaining the daily record of intake and output should be clear. There should of course be daily clinical reevaluation and repetition of the key laboratory studies as often as the patient requires. Sometimes, with large fluid losses, laboratory studies must be repeated every few hours. When a patient's condition has become more stable, every few days may be often enough. The following examples have been chosen to illustrate the evaluation and management of dehydration in two common situations.

CASE 1.—A 62-year-old woman with a 5-year history of aphasia and right hemiparesis following a cerebrovascular accident was admitted because she had been comatose for 24 hours. For 6 months, her family had thought her fluid intake had been inadequate; she had been losing weight, amount unknown. In the past 36 hours she had taken only 120 ml. milk. There had been no vomiting, diarrhea or unusual sweating. Previous blood pressures were unknown. On examination, temperature was normal, pulse 88, respirations Cheyne-Stokes in type, blood pressure 115/70, weight 42 kg. She was only semiresponsive to painful and auditory stimuli. Skin was quite dry with poor turgor, and the tongue was dry. No other physical findings were related to her state of fluid balance. Hematocrit was 41%; catheterization produced 8 ml. of yellow urine which was acid and

gave a strongly positive test for acetone, but contained no albumin or sugar and only a few white cells.

Comment: This patient was clearly dehydrated, and the cause appeared to be a poor intake of fluids for some time and virtually no intake for 2 days. In the absence of any history of abnormal losses of fluid, it seemed likely that her deficit was primarily one of water, but in addition, she probably had a mild deficit of sodium. Her minimal estimated loss of fluid for the preceding 2 days during which she had virtually no intake was about 2.5 L. (600 ml. insensible loss plus 700–800 ml. urine/day).

The serum sodium concentration was elevated to 146 mEq./L., as expected with a primary deficit of water. Serum potassium concentration was 2.7 mEq./L.; this and an electrocardiogram which showed T-wave changes consistent with hypokalemia indicated a significant degree of unexplained potassium depletion.

The oliguria on admission raised the diagnostic alternatives of an easily reversible oliguria due simply to severe dehydration, or the secondary development of acute tubular necrosis or the presence of other renal disease. The absence of abnormalities in the urine suggested little renal damage. A urinary specific gravity would have been helpful, but there was not enough urine. However, the freezing-point depression of this initial urine was determined and was 685 mOsm./kg., a value which is roughly equivalent to a specific gravity of 1.018 for urine of average composition and indicates fairly good concentrating ability. BUN on admission was 19 mg.%. This value excludes severe renal disease but would be consistent with either dehydration or early acute tubular necrosis. Whether the latter was present or not, the patient's dehydration required correction, and indeed only then could this diagnosis be established or excluded. Furthermore, although it is extremely important not to overhydrate a patient with urinary suppression, failure to correct dehydration may be equally serious, since it can cause acute tubular necrosis.

The estimation of the amount of fluid needed to restore this patient to a state of normal hydration was made in two steps, as has been recommended earlier. First, the amount of water required to restore her serum sodium concentration to normal (137 mEq./L.) was calculated, assuming total body water to be 60% of body weight:

A. Total body water $= 0.6 \times 42 = 25.2$ liters.

B. Initial total body water $\times$ initial serum sodium concentration = desired total body water $\times$ desired (normal) serum sodium concentration.

C. $25.2 \times 146 =$ desired total body water $\times$ 137.

D. Desired total body water $= \dfrac{25.2 \times 146}{137} = 26.9$ liters.

E. Water to be added $= 26.9 - 25.2 = 1.7$ liters.

Therefore, the administration of 1.7 liters of dextrose in water

should lower the serum sodium concentration (and total effective osmolality of the body) to normal.

Second, as was estimated above, the total deficit of body fluids was at least 2.5 liters and probably more. Thus, the patient needed 1 or more liters of isotonic sodium solution in addition to the 1.7 liters of water just calculated.

During the 12 hours in which these fluids were to be given, some additional water (about 300 ml.) was needed to replace continuing insensible loss. If urine volume increased, an allowance for this continuing loss would also be needed. Because of the evidence of potassium depletion, it was advisable to give some potassium in the fluids. The fluids actually chosen and given during the first 12 hours were: 5% dextrose in water, 2,000 ml.; 5% dextrose in isotonic saline, 2,000 ml. Each of the last 2 liters of fluid contained 25 mEq. potassium (no potassium was added until the urine flow had increased and it was clear that the patient did not have acute renal failure). At the end of 24 hours, she was more responsive, could take fluids by mouth and appeared better hydrated. She voided involuntarily and the urine output could not be determined. Serum sodium concentration was 139 mEq./L., which agreed well with the value of 137 mEq./L. that our calculations would have predicted if the loss of water in urine during this period was not large. BUN was now 10 mg.%; urinary specific gravity was 1.005; serum potassium concentration remained at 2.7 mEq./L., indicating the need for further administration of this ion.

CASE 2.—A 52-year-old former shipyard worker, paraplegic for 15 years as a result of an accident, was admitted because of an abscess and osteomyelitis in the right hip which required amputation and treatment with antibiotics. In July, 1957, while still in hospital, he began to have more fever and intermittent nausea and vomiting. On July 26, he developed pain in both flanks, hematuria, pyuria and more vomiting. He became lethargic and urine output declined. No obstruction of the urinary tract could be demonstrated.

When his status was re-evaluated on August 2, additional data were obtained from his chart. From 7/15 through 8/1, nurses' notes recorded some vomiting almost every day; he had "copious" drainage from his pelvic wound; hematocrit had been falling steadily and was 29% on 7/27; urinalyses throughout hospitalization showed traces of albumin, many white and red cells, and cultures positive for the same organisms that were isolated from his pelvic abscess; BUN on admission was 11 mg.%; when first repeated, on 7/29, it was 69 mg.%; no weights were recorded. After 7/29, his intake and output were recorded and are shown in Table 12. On examination on 8/2, the findings which pertained to his state of hydration were: poor turgor of the skin with a dry, shrunken tongue; severe thirst; normal vital signs; bilateral costovertebral angle tenderness. Hematocrit was 30%; serum sodium concentration was 122 mEq./L.

Comment: The clinical picture suggested dehydration as a result of vomiting and drainage from the pelvic wound which had been going on for over 2 weeks. By 7/29, he was probably already significantly dehydrated, but the losses of sodium and water had been almost "equivalent" as indicated by the only slightly low value for serum sodium concentration on that day. This would be the expected

TABLE 12*.—BALANCE DATA ON CASE 2

	INTAKE		OUTPUT					
Date	Volume ml.	Na mEq.	Insens. ml.	Urine ml.	Other ml.	Total Vol. ml.	Approx. Na mEq.	Serum Na Conc. mEq./L.
7/29	4,000	150	(700)	2,450	(300) (Dr) 1,400 (V)	4,850	245	130
7/30	3,125	150	(700)	300	(300) (Dr) 950 (V)	2,250	190	
7/31	2,900	75	(700)	250	(300) (Dr) 825 (V)	2,075	170	
8/1	3,000	150	(700)	400	(300) (Dr) 1,000 (V)	2,400	195	
8/2, AM								122
Totals	13,025	525				11,575	800	
8/2	3,000	658	(700)	700	(300) (Dr) 975 (V)	2,675	195	

*Figures in parenthesis represent estimates of insensible loss and drainage from the pelvic wound; thus the total volume of output is also an estimate. (Dr) = drainage; (V) = vomitus. The figure for approximate sodium output is calculated on the reasonable assumption that the serous drainage and vomitus were at a sodium concentration of 150 mEq./L.; no allowance was made for sensible perspiration and there was no way of knowing the losses of sodium in urine.

type of loss from vomiting and serous drainage. If correction of his dehydration had been carried out then, the proper choice would have been isotonic sodium solutions.

The BUN of 69 mg.% on 7/29 and the oliguria thereafter indicated marked impairment of renal function, probably the result of both pyelonephritis and dehydration. The recorded intake and output in the table allow an estimate of fluid balance for that period. From 7/29 to 8/1, there was an estimated *positive* balance of water of 1,450 ml. (13,025 — 11,575) and a *negative* balance of sodium of 275 mEq. (800 — 525). It can be calculated from these balance data

that the serum sodium concentration should have fallen to 118 mEq./L., which is reasonably close to the value actually found, 122 mEq./L.

In the plan for correction of the deficits of sodium and water, the attending physician first calculated the amount of sodium salts needed to raise the serum sodium concentration from 122 to 134 mEq./L. The patient's last recorded weight, just before 7/29, was 56.4 kg. Hence:

A. Total body water about $7/29 = 0.6 \times 56.4 = 34.0$ L.

B. Body water on $8/2 = 34.0 + 1.45$ (positive balance) $= 35.45$ L.

C. Desired increase in serum sodium concentration $= 134 - 122 =$ 12 mEq./L.

D. Total sodium needed $= 12 \times 35.45 = 426$ mEq. Na.

E. Amount of 5% NaCl needed $= \frac{426}{855} = 0.498$ L. or approx. 500 ml.

Note that the calculation was based on the estimated *total* body water.

Thus, the first part of the fluid order for that day (8/2) was 500 ml. 5% NaCl. Other fluids ordered were:

1,000 ml. isotonic NaCl, to match anticipated vomitus.

1,000 ml. dextrose in water, to match anticipated insensible loss and urine (an inadequate amount normally but this figure was chosen because of the oliguria of the preceding 3 days and uncertainty about its reversibility).

500 ml. isotonic NaCl, as a first step toward replacing the unknown amounts of fluid deficit which existed before 7/29.

The balance data for 8/2 are shown in Table 12. On the morning of 8/3, the serum sodium concentration was 130 mEq./L., which is reasonably close to the desired value. His thirst was much less, skin turgor was improved and the urine volume on 8/3 rose to 1,275 ml. Thereafter, the urine volume, with maintenance of adequate hydration, was 2–4 liters daily, and the BUN gradually fell to 33 mg.%. Thus, it appeared that dehydration had contributed to the renal insufficiency and that the latter was partly reversible with correction of fluid balance.

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